THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: Zheng J. Li, et al. :

APPLICATION NO.: 10/650,253 : Examiner: PESELEV, ELLI

FILING DATE: August 27,2003 : Group Art Unit: 1623

TITLE: CRYSTAL FORMS OF AZITHROMYCIN :

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

BRIEF ON APPEAL

Applicants hereby appeal the Office Action mailed March 16, 2006 which finally rejected claims 125 and 128-144. A Notice of Appeal was filed on June 16, 2006. The present Appeal Brief is being filed electronically on August 3, 2006, within two months of the June 16, 2006 Notice of Appeal date. Therefore, the present Appeal Brief is being timely filed.

The Commissioner is authorized to charge the $500 Appeal Brief fee to our Deposit Account No. 16-1445.

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REAL PARTY IN INTEREST

This Application is assigned to Pfizer Inc., a U.S. Corporation organized under the laws of the State of Delaware and having its headquarters at 235 East 42nd Street, New York, New York USA.

RELATED INTERFERENCES AND APPEALS

Applicants would like to direct the Board's attention to pending Patent Interference No. 105,366 (McK) between Zheng J. Li, Andrew W. Trask and Joseph E. Mertz, junior party (Application 10/652,655 and Application 10/650,252) and Claude Singer and Judith Aronhime, Senior party (Patent 6,365,574 and Application 10/816,376).

Applicants note that count 1 of the pending Patent Interference No. 105,366 (McK) includes:

A composition of matter in accordance with claim 124 of Li application 10/652,655

or

a composition of matter in accordance with claim 87 of Li application 10/650,252

or

a composition of matter in accordance with claim 1 of Singer application 10/816,376.

Applicants further note that Claim 124 of Li application 10/652,655 is directed to "A crystalline form of azithromycin, wherein said form is substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate."

Claim 87 of Li application 10/650,252 is directed to "An azithromycin mixture comprising substantially pure azithromycin monohydrate hemi-ethanol solvate characterized as having a plurality of ^{13}C solid state NMR peaks with at least two peaks at approximately 179.5±0.2 ppm and 178.6±0.2 ppm and optionally less than 10% by weight of azithromycin dihydrate characterized as having at least three ^{13}C solid state NMR peaks at approximately 13.2 ppm, 11.3 ppm and 7.2 ppm; wherein said substantially pure azithromycin monohydrate hemi-ethanol solvate contains less than 10% of alternative polymorphic or isomorphic crystalline forms of azithromycin by weight."

Claim 1 of Singer application 10/816,376 is directed to "A non-hygroscopic ethanolate of azithromycin having an ethanol content of about 1.5% to about 3%."

Claim 125 for the present Appeal is "A pharmaceutical dosage form comprising said substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate and a pharmaceutically acceptable carrier or diluent; wherein said crystalline azithromycin

monohydrate hemi-ethanol solvate is characterized as having a ^{13}C solid state NMR spectrum comprising at least one peak with chemical shift of about 179.5 ppm."

Applicants respectfully contend that the subject matter of the present Appeal is patentably distinctive from the count(s) of Interference No. 105,366 (McK) and that the present Appeal be determined on its own merits.

Appellant's legal representative in Patent Interference No. 105,366 (McK) is Connolly Bove Lodge & Hutz LLP, The Nemours Building, 1007 North Orange Street, P.O.Box 2207, Wilmington, DE 19899; Telephone No. (302)658-9141.

Applicants would also like to point out that an Appeal Brief was filed on July 10, 2006 with the Board of Patent Appeals and Interferences in connection with U.S. Patent Application No.10/327,459 (hereinafter "the '459 application"), filed on December 20, 2002. Claim 1 of the '459 application is directed to "A dry blend, used for forming azithromycin tablets by direct compression, comprising: (a) about 1-80%, by weight non-dihydrate azithromycin; (b) at least one pharmaceutically acceptable excipient; and (c) from about 0.25-10%, by weight, of a lubricant; wherein the Carr's Compressibility Index, of the dry blend, is less than about 34%; wherein said nondihydrate azithromycin is azithromycin monohydrate hemi-ethanol solvate."

Applicants respectfully contend that the subject matter of the present appeal is patentably distinctive from the Appeal in U.S. Patent Application No. 10/327,459 and that the Board considers the present Appeal on its own merits.

STATUS OF CLAIMS

1. Claims 125 and 128-144 are pending and currently under appeal. Claims 1-124 and 126-127 have been canceled without prejudice.

2. Claims 125 and 128-144 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement.

3. Claims 125 and 128-144 have been rejected under 35 U.S.C. §102(b) as being anticipated by Bright, U.S. Patent No. 4,474,768.

4. Claims 125 and 128-144 have been rejected under 35 U.S.C. §103(a) as being obvious over Bright, U.S. Patent No. 4,474,768.

5. Claims 125 and 128-144 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Singer et al., U.S. Patent No. 6,365,574 in view of Curatolo et al., U.S. Patent No. 5,605,889.

6. No claims have been allowed.

STATUS OF AMENDMENTS

All amendments have been entered without objection.

SUMMARY OF CLAIMED SUBJECT MATTER

The present invention provides a pharmaceutical dosage form comprising said substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate and a pharmaceutically acceptable carrier or diluent; wherein said crystalline azithromycin monohydrate hemi-ethanol solvate is characterized as having a ^{13}C solid state NMR spectrum comprising at least one peak with chemical shift of about 179.5 ppm. Such a pharmaceutical dosage form was described/defined, *inter alia*, on page 2, lines 14-24, on page 32, lines 25-36, in table 10 on page 25, from line 11 to the end of the page and in example 14 on page 28, lines 24-36 in the original specification.

GROUNDS OF REJECTIONS TO BE REVIEWED ON APPEAL

I. Whether the Examiner erred in rejecting claims 125 and 128-144 under 35 USC §112, first paragraph, as failing to comply with the enablement requirement

II. Whether the Examiner erred in rejecting claims 125 and 128-144 under 35 U.S.C. §102(b) as being anticipated by Bright, U.S. Patent No. 4,474,768 ("Bright")

III. Whether the Examiner erred in rejecting claims 125 and 128-144 under 35 U.S.C. §103(a) as being anticipated by Bright

IV. Whether the Examiner erred in rejecting claims Claims 125 and 128-144 under 35 U.S.C. §103(a) as being unpatentable over Singer et al., U.S. Patent No. 6,365,574 ("Singer") in view of Curatolo et al., U.S. Patent No. 5,605,889 ("Curatolo").

ARGUMENTS

I. Rejection of Claims 125 and 128-144 Under 35 U.S.C. §112, First Paragraph, as failing to comply with the enablement requirement

The Examiner based this rejection on the ground that "there is a good reason to doubt that such crystalline structure can be maintained in an aqueous environment" and that "in so far as the instant claims encompass a dosage form in a dry environment such as a tablet, there is also a good reason to doubt that the claimed product can maintain its crystalline structure under compression. Note the article by Rouhi, (Right Stuff, Chemical and Engineering News, Feb. 24, 2003, pages 32-35)."

Applicants respectfully submit that this rejection is contrary to the law, to the facts and to the current USPTO practice and its standard for interpreting claims on pharmaceutical compositions containing polymorphs in similar cases.

THE EXAMINER FAILED TO FOLLOW USPTO STANDARD FOR CLAIM INTERPRETATION

The current USPTO practice is to grant patents with claims on pharmaceutical compositions containing polymorphs. Applicants have briefly searched the USPTO patent database and found that the Patent Office had indeed granted many patents with claims on pharmaceutical compositions containing polymorphs, including patents examined and allowed by Examiner Elli Peselev. An incomplete list of such patents is shown below according to the Primary Examiner's name:

Examiner Cecilia Tsang:

(1) granted U.S. Patent No. 6,169,108 to Sato et al. of Daiichi Pharmaceutical Co., LtD. on January 2, 2001 wherein its claim 17 is directed to a pharmaceutical composition comprising as an active ingredient the anhydrous crystal according to claim 1; and

(2) granted U.S. Patent No. 5,869,604 to Rousseau et al. of Georgia Institute of

Technology on February 9, 1999 wherein its claim 42 is directed to a biological compound crystal.

Examiner Alan L. Rotman:

(1) granted U.S. Patent No. 6,767,913 to Lifshitz et al. of Teva Pharmaceutical Industries, Ltd. on July 27, 2004 wherein its claim 83 is directed to a pharmaceutical composition comprising clopidogrel hydrogensulfate selected from the group consisting of clopidogrel hydrogensulfate Form III, Form IV, Form V and amorphous form, and a pharmaceutically acceptable excipient.

Examiner Jose G. Dees:

(1) granted U.S. Patent No. 6,482,417 to Leibovici et al. of Teva Pharmaceutical Industries, Ltd. On November 19, 2002 wherein its claim 1 is directed to a stable pharmaceutical formulation comprising an effective amount of high purity torsemide modification II.

Examiner Charanjit S. Aulakh:

(1) granted U.S. Patent No. 6,465,496 to Aronhime et al. of Teva Pharmaceutical Industries, Ltd. on October 15, 2002 wherein its claim 26 is directed to a pharmaceutical composition comprising torsemide Dupont Form 2 ethanol adduct and a pharmaceutically acceptable carrier.

Examiner Fiona T. Powers:

(1) granted U.S. Patent No. 6,605,636 to Aronhime et al. of Teva Pharmaceutical Industries, Ltd. on August 12, 2003 wherein its claim 14 is directed to a pharmaceutical composition comprising the atorvastatin hemi-calcium Form VII or a hydrate thereof of claim 2.

Examiner Elli Peselev:

(1) granted U.S. Patent No. 6,599,884 to Avrutov et al. of Teva Pharmaceutical Industries, Ltd. on July 29, 2003 wherein its claim 14 is directed to a pharmaceutical composition comprising a therapeutically effective amount of clarithromycin Form IV; and

(2) granted U.S. Patent No. 6,936,591 to Dumic et al. of Pliva Pharmaceutical Industry Incorporated on August 30, 2005 wherein its claim 32 is directed to a

pharmaceutical composition comprising substantially pure orthorhombic isostructural pseudopolymorph of 9-deoxo-9a-aza-9a-methyl-9a-homoerythromycin A according to claim 30, and one or more pharmaceutically acceptable excipients.

By granting these patents, the USPTO has established an implied standard of interpreting this type of claims by including the physical characteristic of the polymorph as a claim limitation and these claims do not encompass compositions where the polymorph cannot be detected and/or characterized, such as in an aqueous solution." As applied in the present case, Applicants have specifically included in the claims "wherein said crystalline azithromycin monohydrate hemi-ethanol solvate is characterized as having a ^{13}C solid state NMR spectrum comprising at least one peak with chemical shift of about 179.5 ppm" as an element. One of ordinary skill in the art would easily find out that one cannot obtain solid state NMR spectrum of azithromycin monohydrate hemi-ethanol solvate if it is fully solubilized in a solvent and a claim with a solid state NMR peak as an element would not cover an azithromycin solution. Therefore, the claimed pharmaceutical dosage form would not cover dosage forms where substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate cannot be detected and/or characterized. Accordingly, the full scope of the claims, as being properly interpreted, is fully enabled.

Moreover, this rejection, if not reversed, would harm the public interests by showing the public that USPTO decisions are examiner-dependent. In this case, the same Examiner who allowed claims on pharmaceutical compositions in U.S. Patent No. 6,936,591 on August 30, 2005 would reject the currently claimed pharmaceutical dosage form based on 35 U.S.C. §112, first paragraph. The examiner's decision on whether to grant a patent should be based more on legal principle, USPTO precedents and the examiner's own prior decision, rather than an arbitrary one. Therefore, this ground of rejection should be reversed.

THE EXAMINER ERRED IN DOUBTING THE TRUTH AND ACCURACY OF APPLICANTS' STATEMENT IN VIEW OF ROUHI

The Examiner incorrectly interpreted the disclosure of Rouhi and then erroneously applied the disclosure of Rouhi in this rejection. The Examiner asserted that based on the teaching of Rouhi, the claims pharmaceutical dosage form containing substantially pure azithromycin monhydrate hemi-ethanol solvate are not enabled. Such an assertion cannot be further from the truth.

The correct interpretation of the disclosure of Rouhi is that it deals with the problem of stabilizing polymorphs, i.e., preventing one polymorph from being converted to another. The author defined a polymorph as crystals having identical chemical composition. Such a definition cannot possibly applied to the present application simply because there is only one known polymorph for azithromycin monohydrate hemi-ethanol solvate under the definition of Rouhi, i.e., having azithromycin:water:ethanol ratio of 1:1:0.5. This is clear from the specification and from the cited references. Moreover, the Office Action did not provide any evidence that a second polymorph for azithromycin monohydrate hemi-ethanol solvate can exist, let alone talking about conversion between the first polymorph and the second polymorph of azithromycin monohydrate hemi-ethanol solvate in a solid dosage form. The Examiner has not met her burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright, 999 F.2d 1557, 1562 (Fed. Cir. 1993)* and there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure. *see In re Marzocchi, 439 F.2d 220, 224 (CCPA 1971).*

Even assuming that Rouhi can be used as a reference to support this ground of rejection and further assuming that there is more than one polymorph for azithromycin monohydrate hemi-ethanol solvate, Applicants would still have provided enabling disclosure to the claimed pharmaceutical dosage form because the claimed pharmaceutical dosage form containing substantially pure azithromycin monohydrate hemi-ethanol solvate would include all azithromycin polymorphs having an azithromycin:water:ethanol ratio of 1:1:0.5. The conversion between various polymorphs as defined by Rouhi, even if it exists, does not defeat the enabling disclosure of the claimed pharmaceutical dosage form. Therefore, this ground of

rejection should be reversed.

II. Rejection of Claims 125 and 128-144 Under 35 U.S.C. §102(b) as Being Anticipated by Bright, U.S. Patent No. 4,474,768 ("Bright")

Applicants respectfully submit that the Examiner erred in asserting that Bright anticipate these pending claims. It is clear from the disclosure of Bright that it made a hygroscopic form of azithromycin which was called form B, not substantially pure azithromycin monohydrate hemi-ethanol solvate. Moreover, Dr. Hangac's declaration confirmed that Bright produced azithromycin form B and not substantially pure azithromycin ethanolate. In addition, the pending claims would not cover pharmaceutical compositions where azithromycin monohydrate hemi-ethanol solvate cannot be detected and/or characterized with a ^{13}C solid state NMR spectrum comprising at least one peak with chemical shift of about 178.6 ppm.

Under the case law, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." see *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). Applicants respectfully submit that Bright does not teach each and every element of any of the claims 125 and 128-144. Therefore, Bright does not anticipate any of the claims under appeal and this ground of rejection should be reversed.

III. Rejection of Claims 125 and 128-144 Under 35 U.S.C. §103(a) as Being Obvious Over Bright, U.S. Patent No. 4,474,768

The Examiner bases this rejection on "the reasons set forth in the Office Action of September 12, 2005." The September 12, 2005 Office Action stated that "The declaration by Dr. Hangac has been considered but has not been found persuasive insofar as the claimed pharmaceutical dosage form reads on an aqueous solution since a person having ordinary skill in the art at the time the instant invention was made would not have expected the claimed crystalline azithromycin to maintain its crystal structure. Once dissolved in water, a person having ordinary skill in the art at the time the instant invention was made would have expected the claimed compound and the compound disclosed by Bright to be the same."

For the reasons stated in Applicants' arguments for the reversal of rejection of claims 125

and 128-144 under 35 U.S.C. §102(b), one of ordinary skill in the art would recognize that these claims would not cover an aqueous solution of azithromycin monohydrate hemi-ethanol solvate. Bright does not teach or suggest any pharmaceutical dosage form containing substantially pure azithromycin monohydrate hemi-ethanol solvate. Applicants contend that the Office Action did not satisfy any of the three basic criteria set forth by the Federal Circuit Court in *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991) which states that "to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure." Therefore, this ground of rejection should be reversed.

IV. Rejection of Claims 125 and 128-144 under 35 U.S.C. §103(a) as Being Unpatentable Over Singer et al., U.S. Patent No. 6,365,574 in view of Curatolo et al., U.S. Patent No. 5,605,889

The Examiner bases her rejection in the March 16, 2006 final Office Action on "the reasons set forth in the Office Action of February 7, 2006." The February 7, 2006 Office Action stated that "Singer et al disclose a pharmaceutical composition comprising crystalline monohydrate hemi-ethanol (column 3-4)." The February 7, 2006 Office Action admitted that Singer et al "do not disclose composition in dosage form." The February 7, 2006 Office Action further asserted that "since a pharmaceutical dosage form of azithromycin was well known in the art at the time the instant invention was made as disclosed by Curatolo et al (column 2, lines 35-45), a person having ordinary skill in the art at the time the instant invention was made would have been motivated to prepare the composition disclosed Singer et al in dosage form." The March 16, 2006 final Office Action also stated that "the Declaration by Richard Todd Darrington has been considered but has not been found persuasive since it shows a composition of ethanol solvate in combination with Miglyol 812 but fails to show dosage form of the said composition."

Applicants submit that this rejection for obviousness is contrary to the law, to the facts and to the Examiner's own statement in the February 7, 2006 Office Action.

A COMBINATION OF AZITHROMYCIN ETHANOL SOLVATE WITH MIGLYOL 812 IS A DOSAGE FORM

The Declaration of Richard Todd Darrington clearly stated that he 'participated in the conception and reduction to practice of a pharmaceutical dosage form containing substantially pure Form F Azithromycin" and that "Exhibit 1 describes a pharmaceutical dosage form containing ethanol solvate and a pharmaceutically acceptable carrier, Miglyol 812." Such statements are further supported by two notebook pages. It would be clear and unambiguous to one of ordinary skill in the art that Applicants were in possession of the claimed pharmaceutical dosage form.

In the face of such overwhelming evidence to the contrary, the Examiner still choose to simply assert that a combination of azithromycin ethanol solvate and Miglyol 812 is not a dosage form. The Examiner's assertion also contradicts her own argument in the February 7, 2006 Office Action that "a pharmaceutical dosage form of azithromycin was well known in the art." If a pharmaceutical dosage form of azithromycin is so well-known, the Examiner would not simply assert that a combination of azithromycin ethanol solvate and Miglyol 812 is not a dosage form. One would expect that the Examiner would at least be able to give a reason why she think so on such a well-known subject. The fact of the matter is that the Examiner did not give any reason at all in the Office Action. The Examiner has not met her burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright, 999 F.2d 1557, 1562 (Fed. Cir. 1993)* and there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure. *see In re Marzocchi, 439 F.2d 220, 224 (CCPA 1971).* The Examiner erred on the facts, on the law and on contradicting her own argument in this case. The declaration of Richard Todd Darrington should have been considered for the purpose of removing Singer as a reference against claims 125 and 128-144 because it showed that the date of invention of the subject matter of claims 125 and 128-144 was before May 8, 1998 or before the earliest priority date of Singer. The other reference, Curatolo, does not teach or suggest any pharmaceutical dosage form comprising

azithromycin monohydrate hemi-ethanol solvate and does not render these claims obvious. Therefore, this ground of rejection should be reversed.

THE EXAMINER FAILED TO ESTABLISH
A *PRIMA FACIE* CASE OF OBVIOUSNESS

Even assuming that Singer is considered as a prior art reference against claims 125 and 128-144 and that Singer can be combined with Curatolo, there claims are still nonobvious over the Singer-Curatolo combination because the Office Action failed to establish a prima facie case of obviousness.

The test for proper obviousness rejection is whether the Office Action has satisfied all three basic criteria set forth by the Federal Circuit Court in *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991) which states that:

> to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure.

The Office Action does not meet at least the first and third requirements. Specifically, Singer does not disclose any substantially pure azithromycin monohydrate hemi-ethanol solvate. The Office Action further admitted that Singer does not disclose any dosage form of azithromycin monohydrate hemi-ethanol solvate, let alone any dosage form containing substantially pure azithromycin monohydrate hemi-ethanol solvate. Singer also does not teach that substantially pure azithromycin monohydrate hemi-ethanol solvate in a pharmaceutical dosage form having a ^{13}C solid state NMR spectrum comprising at least one peak with chemical shift of about 179.5 ppm. Applicants note that Example 14 in the original specification was designed "To demonstrate the ability of ^{13}C ssNMR to identify the form of azithromycin contained in a pharmaceutical dosage form." Curatolo does not remedy the deficiencies of

Singer. Therefore, this rejection does not satisfy the third criteria for establishing a *prime facie* case of obviousness under *In re Vaeck.*

Moreover, without looking at the disclosure of the present application, one of ordinary skill in the art would not know from Singer and Curatolo how to obtain the claimed pharmaceutical dosage form comprising azithromycin monohydrate hemi-ethanol solvate having the advantages of maintaining a ^{13}C solid state NMR spectrum comprising at least one peak with chemical shift of about 179.5 ppm. Applicants note that the "suggestion or motivation" criteria must be satisfied from the disclosure of the prior art reference or from the knowledge of persons skilled in the art, not by the use of hindsight in view of the present application (emphasis added). This rejection also does not satisfy the first criteria for establishing a *prime facie* case of obviousness under *In re Vaeck.* Therefore, this ground of rejection should be reversed.

UNEXPECTED RESULTS

Even assuming that the examiner has established a *prima facie* case of obviousness, this ground of rejection should still be reversed under the standard set out by the Federal Circuit Court which has held that "secondary considerations must be given due weight by the examiner and Board of Appeals during ex parte prosecution." *In re Sernaker*, 702 F.2d 989, 217 (Fed. Cir. 1983). Applicants contend that the examiner failed to give due weight to secondary considerations, such as unexpected/superior results.

The September 12, 2005 Office Action stated on page 4 that "insofar, as the instant claims encompass a dosage form in a dry environment such as a tablet, there is also a good reason to doubt that the claimed product can maintain its crystalline structure under compression. Note article by Rouhi, "Right Stuff", Chemical and Engineering News, Feb., 24, 2003, pages 32-35 (hereinafter "Rouhi"). According to that article, it is an enormous challenge to manufacturers as to how a favorable polymorph can be maintained in a pharmaceutical composition." Applicants respectfully contend that Rouhi should be given, at least, the objective evidence status because it was used by the examiner to reject the presently pending claims. Such objective evidence is entitled to great weight in a case. *see Rosemount, Inc. v. Beckman Instruments, Inc.*, 727 F. 2d 1540 (Fed. Cir. 1984).

Based on the prior arts and the Examiner's interpretations of the prior arts, such as

Rouhi, the expectation in the art would be that drug crystals would convert to other crystal forms in dosage forms. Applicants, however, unexpectedly obtained a pharmaceutical dosage form containing substantially pure azithromycin monohydrate hemi-ethanol solvate. Applicants not only obtained a pharmaceutical dosage form containing substantially pure azithromycin monohydrate hemi-ethanol solvate, but also a pharmaceutical dosage form having a ^{13}C solid state NMR spectrum comprising at least one peak with chemical shift of about 179.5 ppm. Such "unexpected results" are evidence of nonobviousness under M.P.E.P. § 716.02 (a)(III) and should be given due weight under the Federal Circuit Court's holding in *In re Sernaker*, 702 F.2d 989, 217 (Fed. Cir. 1983). Therefore, claims 125 and 128-144 are nonobvious over Singer in view of Curatolo. Accordingly, this ground of rejection should be reversed..

SUMMARY

The rejection of the claims 125 and 128-144 under 35 USC §103(a) over Singer in view of Curatolo is contrary to the facts, the case laws and the examiner's own arguments. Singer is not a proper reference against claims 125 and 128-144. Even assuming Singer can be cited against these claims and that Singer can combined with Curatolo, the Office Action failed to establish *prima facie* obviousness. Therefore, this ground of rejection should be reversed.

CONCLUSION

For the foregoing reasons Applicants respectfully request that the rejections of claims 125 and 128-144 be reversed.

It is believed that no fee, other than the $500 Appeal Brief fee, is deemed necessary in connection with the filing of the present Appeal Brief. However, if any other fees are required, the Board is hereby authorized to charge any such fees to our Deposit Account No. 16-1445.

Respectfully submitted,

Date: August 3, 2006

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CLAIMS APPENDIX

1 - 124. (CANCELED).

125. (PREVIOUSLY PRESENTED) A pharmaceutical dosage form comprising said substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate and a pharmaceutically acceptable carrier or diluent; wherein said crystalline azithromycin monohydrate hemi-ethanol solvate is characterized as having a ^{13}C solid state NMR spectrum comprising at least one peak with chemical shift of about 179.5 ppm.

126-127. (CANCELED)

128. (PREVIOUSLY PRESENTED) The pharmaceutical dosage form of claim 125, wherein said substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate is characterized as having a ^{13}C solid state NMR spectrum further comprising a peak with chemical shifts of about 178.6 ppm.

129. (PREVIOUSLY PRESENTED) The pharmaceutical dosage form of claim 128, wherein said substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate is characterized as having a ^{13}C solid state NMR spectrum further comprising a peak with chemical shifts of about 58.0 ppm.

130. (PREVIOUSLY PRESENTED) The pharmaceutical dosage form of claim 129, wherein said substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate is characterized as having a ^{13}C solid state NMR spectrum further comprising a peak with chemical shifts of about 17.2 ppm.

131. (PREVIOUSLY PRESENTED) The pharmaceutical dosage form of claim 130, wherein said substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate is characterized as having a ^{13}C solid state NMR spectrum further

comprising a peak with chemical shifts of about 10.1 ppm.

132. (PREVIOUSLY PRESENTED) The pharmaceutical dosage form of claim 131, wherein said substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate is characterized as having a ^{13}C solid state NMR spectrum further comprising a peak with chemical shifts of about 9.8 ppm.

133. (PREVIOUSLY PRESENTED) The pharmaceutical dosage form of claim 132, wherein said substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate is characterized as having a ^{13}C solid state NMR spectrum further comprising a peak with chemical shifts of about 9.3 ppm.

134. (PREVIOUSLY PRESENTED) The pharmaceutical dosage form of claim 133, wherein said substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate is characterized as having a ^{13}C solid state NMR spectrum further comprising a peak with chemical shifts of about 7.9 ppm.

135 (PREVIOUSLY PRESENTED) The pharmaceutical dosage form of claim 134, wherein said substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate is characterized as having a ^{13}C solid state NMR spectrum further comprising a peak with chemical shifts of about 6.6 ppm.

136. (PREVIOUSLY PRESENTED) The pharmaceutical dosage form of claim 125, wherein said substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate comprises 82% or more by weight of crystalline azithromycin monohydrate hemi-ethanol solvate.

137 (PREVIOUSLY PRESENTED) The pharmaceutical dosage form of claim 125, wherein said substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate comprises 84% or more by weight of crystalline azithromycin

monohydrate hemi-ethanol solvate.

138. (PREVIOUSLY PRESENTED) The pharmaceutical dosage form of claim 125, wherein said substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate comprises 86% or more by weight of crystalline azithromycin monohydrate hemi-ethanol solvate.

139. (PREVIOUSLY PRESENTED) The pharmaceutical dosage form of claim 125, wherein said substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate comprises 88% or more by weight of crystalline azithromycin monohydrate hemi-ethanol solvate.

140. (PREVIOUSLY PRESENTED) The pharmaceutical dosage form of claim 125, wherein said substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate comprises 90% or more by weight of crystalline azithromycin monohydrate hemi-ethanol solvate.

141. (PREVIOUSLY PRESENTED) The pharmaceutical dosage form of claim 125, wherein said substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate comprises 94% or more by weight of crystalline azithromycin monohydrate hemi-ethanol solvate.

142. (PREVIOUSLY PRESENTED) The pharmaceutical dosage form of claim 125, wherein said substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate comprises 98% or more by weight of form F azithromycin.

143. (PREVIOUSLY PRESENTED) The pharmaceutical dosage form of claim 125, wherein said substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate comprises 99% or more by weight of form F azithromycin.

144. (PREVIOUSLY PRESENTED) The pharmaceutical dosage form of claim 125, wherein said dosage form comprises from about 1.0% to about 70% of substantially pure crystalline azithromycin monohydrate hemi-ethanol solvate.

EVIDENCE APPENDIX

Chemical AND Engineering News
February 24, 2003
Volume 81, Number 8
CENEAR 81 8 pp. 32-35
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THE RIGHT STUFF

From research and development to the clinic, getting drug crystals right is full of pitfalls

EYE-CATCHING The beauty of a highly metastable form of paracetamol is revealed when viewed between crossed polarizers on a hot-stage microscope.
PHOTO BY HELGE RIXNER/SOLVIAS

A. MAUREEN ROUHI, C&EN WASHINGTON

The next time you must swallow a drug tablet, take a moment to inspect it. Is it whole? Dust free? Is it uniform in composition? Very likely, you'll find every time that it is. We expect tablets to be like that, and we take them without second thoughts. Yet to produce something as prosaic as a tablet requires chemical and engineering decisions that must take into account not only safety, efficacy, and processibility but also defensibility of intellectual property.

The drug substance is the most important ingredient in that tablet but not necessarily the one in greatest amount; other components, called excipients, make up the rest. Most drug substances--or active pharmaceutical ingredients (APIs)--are solid organic compounds, even though the final drug product may be in liquid form. Thus, the formation of solids of uniform properties is critical in API production. Failure to do so can be devastating.

The case of ritonavir, Abbott Laboratories' drug for patients with AIDS, is well known. The drug was formulated as an encapsulated solution in ethanol/water. In the summer of 1998, supplies were threatened when a new crystal form appeared, first at a production plant in North Chicago and then at a plant in Italy. Ritonavir was the victim of a late-appearing polymorph

with different solubility properties.

Polymorphs arise when molecules of a compound stack in the solid state in distinct ways. Although identical in chemical composition, polymorphs can have very different properties. They are distinguishable by various analytical techniques, especially X-ray powder diffraction. In addition, solids may form solvates and hydrates, also called pseudopolymorphs.

Polymorphs tend to convert from less stable to more stable forms. The rate of conversion depends on the required activation energy and the differences in free energies, says Wayne J. Genck, president of Genck International, an industrial consulting group based in Richton Park, Ill., that specializes in crystallization and precipitation. But no method yet exists to predict the polymorphs of a solid compound with significant certainty. The search for polymorphs is largely an empirical exercise.

"It is still not possible to figure out how many different ways a molecule can lie down with itself in a lattice," says Jerry L. Atwood, a chemistry professor at the University of Missouri, Columbia. "Small-molecule drugs are very flexible. There's no way to tell what a large floppy molecule can do in the solid state except by doing experiments. It gets worse when you consider that this molecule might have nonobvious binding sites for solvent molecules."

Predictive software systems are available but are restricted in the size and elemental compositions of the molecules they can handle, says G. Patrick Stahly, chief operating officer of SSCI, a West Lafayette, Ind.-based cGMP (current Good Manufacturing Practice) contract research laboratory. It specializes in chemistry, crystallization, and characterization of solid materials. "Even when crystal structures can be predicted, the relatively small energy differences between polymorphs make it difficult to predict which calculated structures are likely to be real," he adds.

Experiments to find polymorphs typically reveal the more stable forms first, Stahly says. Sometimes the less stable forms--also called metastable forms--may be encountered first, but that is not usual, he adds.

It is best to work with the most stable polymorph--also called the ground-state form--because it will not convert any further. But the ground state usually is the least soluble. To improve bioavailability, drug companies sometimes trade off polymorph stability with solubility, "recognizing that they will have to deal with the possibility of an undesired conversion to a more thermodynamically stable form," Genck says.

"It is still not possible to figure out how many different ways a molecule can lie down with itself in a lattice."

ON THE OTHER HAND, Stahly says that much effort is being expended looking for metastable forms of currently marketed drugs whose stable forms have been around for a long time. For innovator companies, new forms offer the possibility of introducing improved drug products. For generic companies, new forms present an opportunity to make generic versions of brand-name products more quickly.

When polymorph conversion occurs, it may be impossible to reproduce the less stable form. It just disappears. Tales of disappearing polymorphs abound. Evelyne Chassagneux, director of business development at Archemis, a French contract development organization, recalls a drug candidate for which Phase I clinical trials had just been completed when a new polymorph appeared. "The properties changed, and we never recovered the old form," she tells C&EN. Fortunately, the conversion occurred at an early stage in development. "The lost form was not registered. If it had been registered, all the work would have had to be redone. That would have been a disaster."

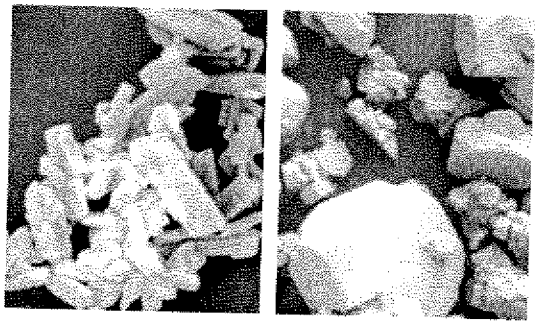
Furthermore, in this case, the late-appearing polymorph fortuitously had better processing qualities. "The old crystals were needlelike, very sticky, with lots of static electricity," Chassagneux says. "The new form was easier to formulate."

The outcomes for ritonavir were different. From solubility and manufacturing perspectives, the old form was superior to the new form, and Abbott process chemists worked mightily to recover it. Not only did they develop a method that ensured consistent production of the old form only, but they also found a way to convert the new form to the old form.

San Kiang, director for process R&D at Bristol-Myers Squibb's Pharmaceutical Research Institute, New Brunswick, N.J., tells about a similar outcome for a compound that had been in development for 10 years. "The sky dropped one day--a new polymorph was discovered in the pilot plant," he says. In this case, putting the pilot plant under quarantine and imposing manufacturing protocols like those for operating under sterile conditions allowed production of the old form to continue, he says. The drug product now in the market contains the original polymorph, he adds.

"Different polymorphs differ in bioavailability, solubility, dissolution rate, chemical and physical stability, melting point, color, filterability, density, and flow properties, among others," Stahly says. The difference in solubility can affect drug efficacy, bioavailability, and safety.

Stahly cites a case in which test animals survived the first toxicological test of a drug candidate but died in the second. "Subsequent analysis showed that the first test was carried out using a crystalline form of the drug and the second using an amorphous form." he says. "Amorphous forms can be up to 1,000 times more soluble than the crystalline form," he explains. Because of that solubility advantage, amorphous forms are preferred for some formulations, such as drugs that will be reconstituted to an injectable solution. But because the amorphous form is always under thermodynamic pressure to crystallize, a frequent problem is crystallization over time.



GOOD LUCK The disappearance of the polymorph characterized by needlelike particles and poor flowability (left) upon formation of the polymorph characterized by big-faceted crystals and good processibility was fortuitous.
COURTESY OF ARCHEMIS

IN ANOTHER EXAMPLE, a change in the equipment used to dry the final drug substance gave a product that had inferior handling and filtering properties than what the manufacturer was used to. The new drying equipment was causing the formation of hydrates. "This case is interesting because it shows that control of form was occurring at the drying stage," Stahly says. "That's one of the last places people look. Most people think that the critical stage is when the crystals come out of solution. But there are many places after crystallization where changes can occur," he explains.

Polymorphs are also important in formulation and storage, according to Rolf Hilfiker, head of the physical chemistry business unit of Solvias, the Basel, Switzerland-based custom research company that was spun off from Novartis. Some polymorphs are more difficult to formulate than others because of their shape or hygroscopicity. And "what's really important during storage is not to have a conversion from one form to another. Otherwise, your tablet will turn either into powder or into concrete. It won't have the same bioavailability anymore," he says.

Even with intermediates for API synthesis, polymorphism is an issue, says Genck. Although intermediates eventually end up being dissolved--and once they are dissolved, polymorphism is no longer an issue--they are supplied as solids. At this stage, the issue is not so much stability but processibility, Genck says. Metastable forms sometimes reject impurities and filter better than the most stable polymorph.

Kiang recalls a recent incident in the manufacture of an intermediate. "One of the impurities had always been an oil," he explains. "It never crystallized, so it was easily eliminated during processing. But one day, it crystallized and became an impurity in the product. It took a lot of process redesigning to eliminate this new crystal, which had never formed before."

Despite the compelling case for polymorphism studies early in drug development, the practice is not standard in the pharmaceutical industry. "There are two types of companies," Chassagneux says. "Those that have already experienced problems do the studies very early. They have learned their lesson. The others don't pay attention. When they have problems, they ask us to troubleshoot."

The pharmaceutical industry has not really had a good handle on issues of crystallization and polymorphism, says Allan S. Myerson, a professor of chemical engineering at Illinois Institute of Technology, Chicago. Myerson directs the Particle Technology & Crystallization Center at IIT. The center is a collaboration of IIT, Purdue University, and Massachusetts Institute of Technology that was established last year to address basic problems in crystallization and particle technology relevant to the pharmaceutical industry.

"We're focusing our effort on the API," Myerson says. "That includes polymorphism, crystal shape, crystal size, understanding what data are required on a very small scale to make the same material repeatably on a larger scale, interaction of API with excipients, and how unit

operations--such as granulation, compaction, and tableting--affect crystal structure."

The center is funded by subscriptions from member companies, which at present number three: Abbott, Aventis, and Bristol-Myers Squibb, Myerson says. Currently, three projects are under way: developing methods for seeding, evaluating techniques for online sensing of crystallization parameters, and studying the interaction of APIs with excipients.

DRUG COMPANIES have urgent reasons to systematize knowledge in these areas, Myerson says. First, the Food & Drug Administration has become very strict about API form, shape, and size distribution, especially after the generic drug scandal of the late 1980s. Patients taking some generic drugs were not getting the therapeutic effect because the API in the generic version was a different polymorph and had poorer solubility and bioavailability than that in the brand-name drug.

SCRUTINY The search for polymorphs requires rigorous visual inspection. PHOTO COURTESY OF SSCI

Second, mistakes can cost hundreds of millions of dollars.

Ritonavir is well-known, but many other cases of new polymorphs appearing at late stage are not made public, Myerson says. "It is very expensive to go back, reformulate, and do your testing again."

Companies constantly have scale-up problems, often because they haven't done the correct experiments on a small scale and they don't have the appropriate fundamental data for developing a crystallization process, Myerson says. "It's shocking sometimes, but drug companies have so many precandidate compounds that the strain in getting data early has led them to not get as much. When suddenly one of these compounds becomes hot and they have to make more of it, they go without basic data."

And third, polymorphs have patent implications.

Polymorphs can be patented if they can be shown to have better properties than others, Hilfiker says. For maximum patent protection, drug companies usually patent the compound first, and then they do the studies to find the polymorphs and patent those as well. "It's dangerous to wait too long because somebody else can come in and patent the good polymorphs first," he adds.

Polymorphs and pseudopolymorphs have been central to a number of legal cases between innovator and generic drug companies. For example, efforts by GlaxoSmithKline to protect the antidepressant Paxil (paroxetine hydrochloride) from generic competition have been based in

part on separate patents claiming anhydrous and hemihydrate forms of the drug substance. Similarly, GSK has claimed extended patent protection of the acid reflux drug Zantac (ranitidine hydrochloride) on the basis of a new crystal form patented eight years after the drug substance patent was issued.

In another example, Bristol-Myers Squibb sued a generic company marketing a hemihydrate of the antibiotic cefadroxil. BMS claims the monohydrate in a patent, and it sued on the basis that the hemihydrate converts into the monohydrate transiently before it dissolves. "To most scientists, realizing that the drug itself is undoubtedly not hydrated when it is in the active site and doing its job, this argument is highly creative," Atwood notes. The case was decided against BMS because it did not prove that the conversion in vivo occurs as claimed.

These cases underscore the difficulty of properly characterizing compositions of matter so that a patent not only claims as much as possible and substantiates all the areas under the claim, but also protects the intellectual property from attack. Typically, the scientist writes up the invention, and the legal team takes the lab notebook and translates the invention into a patent, Atwood says. If the legal team does not understand the subtle nuances of the scientist's methods, the product will be vulnerable to attack. It is precisely at that time when no one yet knows whether a patent may be worth billions--or nothing--when a few dollars and some outside help can save a blockbuster from attack in later years, he says.

Polymorphs have so much impact that it makes sense to do polymorphism studies early on, Hilfiker says. "We advise a small study at preclinical development and a large study before clinical studies."

Compared with the total cost of drug development, the cost of polymorph screening is minuscule: from $25,000 to $100,000, depending on the scope, Stahly says. The experiments are designed to encourage the production of different forms based on variations in nucleation and growth conditions. A screen that incorporates impurities and degradation products is recommended for drug candidates in an advanced stage of development.

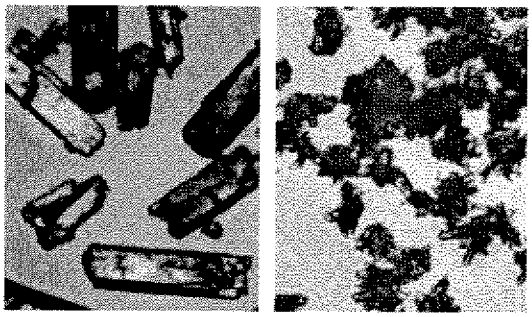
"The primary lesson we took from the ritonavir case was that the effects of impurities and degradation products should be investigated during screening," Stahly says. That's because Abbott chemists showed that the late-forming polymorph was induced by the presence of a ritonavir degradation product with a very similar conformation.

Screening can never give 100% of the possible polymorphs. As many in the field like to say, the number of polymorphs increases with the length of time a compound is under scrutiny. "It's not just that the screening fails," Bristol-Myers Squibb's Kiang explains. "When you're optimizing the process to make the active substance, you are changing chemicals and reaction conditions. Those changes in the normal course of development may surprise you with a new polymorph that didn't show up in the screen."

Kiang offers a simple strategy to minimize the possibility of late-appearing polymorphs: Fix the last step first. "You know your target from day one," he says. "How to get there is up to the imagination of the chemist. But you can decide at the outset what the final chemical step will be, and you can design it to be as chemically simple as possible and optimize conditions to get the

same polymorph every time."

If you can't fix the final step, then add a recrystallization step, Kiang says. "It sounds redundant, and you always lose yield with each step," he adds. "But for some compounds, such as very potent compounds or compounds that must be formed as very fine particles, it may be the best approach."



CONTROL Crystals formed by ultrasound-initiated nucleation (left) are better defined and more processible than those produced without ultrasound. (Photos taken under the same magnification.)
PHOTO COURTESY OF ACCENTUS

VARIOUS TECHNIQUES and strategies are available to get particles of desired characteristics. "I call it particle engineering," Kiang says. "Given the salt form, the polymorph, the requirements of the formulation, ask yourself what are the desired properties of the crystals. We now have various techniques and approaches to achieve those properties through crystallization."

Particles of submicrometer size can be achieved with very fast mixers and high-shear mixers. Additives may be added during crystallization to modify the crystal shape for processibility. "Most drug substances crystallize as needles," Kiang explains. "Needles don't flow very well, but we can force them to change shape through engineering."

Another tool is available from Accentus, Abingdon, England: a scalable, noninvasive technology to control crystal habit and size distribution based on ultrasound.

Sonocrystallization--or crystal formation through ultrasound--has been around for a long time in the lab, says Linda J. McCausland, Accentus chief technologist. The problem has been in scaling up systems based on metal probes sticking into crystallizers. "That doesn't work because you tend to get hot spots," she says. "The ultrasound is thrown just a couple of centimeters from the probe tip instead of throughout the reactor. Plus, the probe erodes, giving all kinds of contamination problems."

In the Accentus design, ultrasound is delivered through transducers bonded onto the outside walls of a flow cell. The flow cell may be configured with the crystallizer in two ways. In a batch mode, it is connected through a tube through the crystallizer lid. When the crystallizer contents are ready for seeding, an aliquot is sent up to the flow cell by vacuum or pressure and treated for the period required to form the desired crystal seeds. Then the seeds are dropped back to the bulk. This setup is used when the goal is to use ultrasound to produce seed crystals

only.

In a continuous mode, the flow cell is connected to the crystallizer in a loop. Material from the bulk enters the loop, is treated in the flow cell, and then circulates back to the crystallizer. This setup is used when the bulk needs to be treated with ultrasound to control size distribution. McCausland says both modes have been scaled up to 4,500 L.

According to Peter W. Cains, a senior chemist at Accentus, there is evidence that use of ultrasound to nucleate potentially polymorphic systems likely forms either the ground-state polymorph or one near the ground state. Where this can be very useful is when a drug candidate has been screened for polymorphs and a potential ground state has been identified. "We can run tests with ultrasound and see if we can get a more stable polymorph," McCausland says.

But Cains cautions: "You can never prove that any technique produces the ground state. In a lot of development projects, you don't know what the ground state is."

"The worst thing is bringing to market a metastable form and not knowing it," Hilfiker says, referring back to the ritonavir case. "If Abbott had known, it may not have used that form. Or it would have developed a process that would have precluded polymorph conversion."

Polymorphism And Crystallization Must Be Mastered From Start To Finish

A. MAUREEN ROUHI, C&EN WASHINGTON

Polymorphism studies encompass a variety of activities and technologies. According to G. Patrick Stahly, chief operating officer of SSCI, a contract research laboratory in West Lafayette, Ind., projects generally fall into one of four categories.

SELECTING THE SOLID FORM. This is usually done at the later stages of discovery so that the material used in toxicology, clinical formulation, and process studies is the right one from the beginning. Solid form selection involves two stages. The first is salt selection, to determine whether the drug should be produced as an acidic or basic salt or as a neutral compound. The second is polymorph screening, where solid samples are generated under diverse conditions and each sample is characterized by X-ray powder diffraction (XRPD) or other techniques to determine polymorphs.

The polymorphs are further characterized by other analytical techniques such as differential scanning calorimetry, hot-stage optical microscopy, and Raman and infrared spectroscopy. The goal is to understand the thermodynamic relationships of the polymorphs, predict their stabilities, and select the best solid form to be used.

DEVELOPING AN ANALYTICAL METHOD. Drug companies must monitor the polymorph in the drug product to ensure that it persists during manufacture. Qualitative and quantitative methods are needed to analyze solid mixtures, sometimes under cGMP (current Good Manufacturing Practice) conditions. Methods must be developed for various types of formulations (tablets, microspheres, transdermal patches, stints, slurries, and lyophile cakes).

DESIGNING A CRYSTALLIZATION PROCESS. A method to make the right polymorph and a procedure to formulate that form into a stable drug product will reduce time to market. On the basis of the thermodynamic stabilities of the polymorphs and their equilibrium solubilities across the temperature range to be used in manufacturing and formulation, a crystallization is designed to produce the required polymorph by batch or continuous processing.

TROUBLESHOOTING. Problems that crop up include out-of-control crystallization, change in product stability, migration of ingredients within structured tablets, and polymorph conversion during manufacture. Sophisticated techniques often are needed in troubleshooting. Spectroscopic and XRPD mapping are particularly useful in providing a 2- or 3-dimensional representation of the polymorph content within selected areas of the product.

RELATED PROCEEDINGS APPENDIX

Memorandum of Senior Administrative Judge, Fred E. McKelvey dated December 16, 2005 and his Standing Order (copies enclosed).

There has been no decision in connection with the Appeal Brief filed on July 10, 2006 with the Board of Patent Appeals and Interferences in U.S. Patent Application No.10/327,459 (hereinafter "the '459 application"), filed on December 20, 2002.

Paper 3

Filed by:

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Filed 16 December 2005

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES
(Senior Administrative Patent Judge McKelvey)

ZHENG J. LI, ANDREW W. TRASK and JOSEPH E. MERTZ,

Junior Party
(Application 10/652,655 and
Application 10/650,252),

v.

CLAUDE SINGER and JUDITH ARONHIME,

Senior Party
(Patent 6,365,574 and
(Application 10/816,376).

Patent Interference 105,366 (McK)
Technology Center 1600

MEMORANDUM

A. Declaration of interference

1. The parties are advised that the Li applications have been withdrawn from issue at the direction of Technology Center 1600.

2. An interference is declared (35 U.S.C. § 135(a)) involving (1) two Li applications versus (2) a Singer patent and a Singer reissue application.

3. The details of the applications and patent appear in the DECLARATION.

B. Discussion

1. During what is supposed to be "ex parte" prosecution of the Li applications and "ex parte" prosecution of the Singer reissue application, there has been considerable "inter partes-like" back-and-forth "debate" between Li and Singer as to whether there is an interference.

2. The back-and-forth debate during so-called "ex parte" prosecution has been made possible due to Public PARE.

3. As one examiner has recently noted: Public PARE allowes attorneys to badger examiners.

4. This case tends to show that the examiner may have a point.

5. Personnel in Technology Center deserve a lot of credit for being able to keep up with the back-and-forth which occurred in this case, all the while making every attempt to pay attention to, and keep up with, all the other numerous cases on the docket of Technology Center 1600.

6. What about the back-and-forth in this case?

7. As an example, in a DECLARATION OF JUDITH ARONHIME PURSUANT TO 37 C.F.R § 1.132, received by the PTO on 8 September 2005, a discussion is presented, together with an analysis, urging the PTO to (see page 8):

(1) conclude that the azithromycin ethanolate disclosed and claimed in the Singer reissue is the same solid state form as azithromycin Form F disclosed and claims in the Li applications and

(2) declare an interference.

8. With what can only be characterized as "lightning speed", Li responded to the Aronhime declaration.

9. Thus, (1) within a four-day period (which incidently included a Saturday and Sunday) of the PTO's receipt of the Aronhime analysis, and (2) in a FIFTH SUPPLEMENTAL RESPONSE received on 12 September 2005 in Li application 10/652,655, Li presents a counter-argument to the effect that no interference can possibly exist between Li and Singer.

10. In support of the argument, Li relies on a Quallich DECLARATION UNDER RULE § 132 filed on 12 September 2005.

11. Quallich was not impressed with the Aronhime analysis.

12. Instead, Quallich urges that the azithromycins of Singer and Li are not even remotely the same.

13. It did not take long for Singer to respond to the Quallich declaration.

14. On 30 September 2005, the PTO received a SUPPLEMENTAL RESPONSE, which it will be noted was preceded by an interview with the examiner said to have taken place on 28 September 2005 (Page 2, second full ¶).

15. In the SUPPLEMENTAL RESPONSE, Singer sets out through argument of counsel to convince all who will listen that Quallich has missed the boat.

16. Despite all the "ex parte" back-and-forth, what cannot be overlooked by any disinterested observer, such as officials in Technology Center 1600 and the board, is the fact that neither Li nor Singer have undertaken any attempt to:

(1) repeat its own experimental work and the experimental work of the "opponent",

(2) make a comparison of apples to apples and

(3) favor the PTO with an analysis of that comparison.

17. Instead, the two sides present argument and evidence which has all the appearance of being comparable to two ships passing in the night, the only difference being that ships tend to pass each other quietly.

18. After a consideration of the "ex parte" evidence, and recognizing at this time that it has not been subject to cross-examination, the PTO has to do the best it can.

19. To be sure, the PTO does not have laboratory to do the work which the "parties" could have done during ex parte prosecution.

20. At the end of the day, the PTO currently finds that the Aronhime "testimony" is entitled to more weight than the contrary Quallich "testimony".

21. To the extent that the Aronhime "testimony" conflicts with that of Quallich, the PTO credits the Aronhime "testimony" over the Quallich "testimony."

22. Resolving the conflicting Aronhime "testimony" and Quallich "testimony" in favor of Aronhime, leads the PTO to find that, on the record before it, there is an interference.

23. Therefore, an interference is declared.

24. The declaration of an interference creates presumptions, including presumptions that (1) there is an interference-in-fact and (2) the claims of the parties are supported by an enabling disclosure.

25. The parties are free to attack these presumptions, but must do so with convincing evidence.

26. In an interference, a party attacking a presumption has the burden of proof.

27. The parties are urged to carefully review the STANDING ORDER and take due note of the fact that opinions of experts which are not supported any convincing underlying basis may not be given any weight.

28. Moreover, the parties are advised right up front that the board will not sift through mountains of evidence trying to figure out if the evidence somehow might support a party's position.

29. Rather, a party filing a motion should know that it must present a set of facts, supported by specific references

to specific evidence and an argument which the board can follow logically to a conclusion the party wants the board to reach.

30. We will not, and do not, take on the role of an advocate for either party.

31. Various scientific tests are mentioned in the specifications of both parties.

32. For example, Singer mentions powder X-ray diffraction. See Fig. 2.

33. Other tests are mentioned in column 3 of the Singer patent.

34. Li also mentions powder X-ray diffraction, but also refers to ^{13}C solid state NMR spectrum. See, e.g., Fig. 23 and page 9 of the specification.

35. In the event the parties rely on these and other test protocols, then the parties are well advised to take due note of the portion of the STANDING ORDER setting out how a party should describe a test and its significance.

C. Motions authorized at this time

1. No imagination is necessary to see that at least Li will urge that there is no interference-in-fact.

2. Hence, at least Li is authorized to file a motion for judgment based on no interference-in-fact.

3. Although it does not seem likely, Singer is also authorized to file a motion for judgment based on no interference-in-fact.

4. Moreover, based on what the board perceives as each party's less than charitable view of their opponent's specification, it seems manifest that motions for judgment based on alleged lack of enablement are a foregone conclusion.

5. Accordingly, each party is also authorized to file a motion for judgment based on alleged lack of enablement (35 U.S.C. § 112, first paragraph).

6. All other motions which a party would like the board to authorize should be listed in the motions list.

7. Time Period 1 in this interference will be set right now to expire on **Tuesday, 28 February 2006.**

8. Given the parties ability to react with unusual speed before the examiner, a 28 February 2006 deadline should pose absolutely no problem.

9. Other times will be set at a future date.

10. What about the fact that Li is considerably "junior" to Singer and the requirements of 37 CFR § 41.202(d) (2005)?

11. For the time being, given that a motion for judgment based on no interference-in-fact will probably surface from at least Li, the board will hold in abeyance requiring Li to show how it can prevail on priority.

/ss/Fred E. McKelvey
FRED E. McKELVEY,
Senior Administrative Patent Judge[1]

16 December 2005
Alexandria, VA

[1] As part of board efforts under the government Paperwork Elimination Act, signatures on papers originating from the board have been phased out in favor of a completely electronic record. Consequently, in this case papers originating at the board will not have signatures. The signature requirements for the parties have not changed. See, e.g., 37 CFR § 10.18.

cc (via fax and overnight delivery):

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United States Patent and Trademark Office

Before the Board of Patent Appeals and Interferences
(Interference Trial Section)

13 September 2004

STANDING ORDER

This Order is promulgated by and for the Trial Section under Bd. R. 104 for use in contested cases.

CONTENTS

¶ 1 Notice of confidential information

Some opinions are selected for publication to promote public understanding of Trial Section practice or to create uniform practices. If a party believes that its application contains information not otherwise publicly available that should be redacted from any opinion, the party must **within two (2) months** of the initiation of the contested case file as a separate paper a notice specifically identifying such information.

If additional information not otherwise publicly available is introduced into a contested case that a party believes should be redacted from any opinion, the party must promptly file a notice specifically identifying the information.

If, after filing such notice, specifically identified information becomes publicly available (for example, through publication of a collateral application), the party shall promptly notify the Board of this change in the status of the information.

¶ 2 Record management

¶ 2.1 Letters between counsel not to be filed

No letter between counsel may be filed unless it is filed as an exhibit cited in a motion, opposition, or reply, or during cross-examination.

¶ 2.2 No duplicate papers

A party may not file (not even as an appendix or exhibit) a copy of a paper previously filed in the same contested case.

¶ 3 Mandatory notices

¶ 3.1 Real party-in-interest

Within **fourteen (14) days** of the date of the Declaration, each party must file as a separate paper a notice of any and all right, title, or interest in any application or patent involved in the contested case.

¶ 3.2 Related proceedings

Within **fourteen (14) days** of the initiation of a contested case, each party must file and serve as a separate paper a notice identifying the application or patent number of every United States application or patent claiming, or which may claim, the benefit of priority of the filing date of the party's involved patent or application. If there are no such applications or patents the notice must state this fact. If, during the course of the proceeding, a party files an application claiming, or which may claim, the benefit of the filing date of an involved application or patent, a notice of the filing, including the application number, must be promptly served and filed.

¶ 4 Communications with the Board

¶ 4.1 Default mode

Mail is the default mode of communication.

¶ 4.2 Filing by hand

Hand delivery to the Board must occur between the hours of 8:30 a.m. and 5:00 p.m at:[*]

Madison Building East, 9th Floor
600 Dulany Street
Alexandria, Virginia 22314

Any paper hand-delivered directly to the Board before 10:00 a.m. is deemed to have been filed the previous business day provided the paper was properly served the previous business day.

¶ 4.3 Overnight delivery services

Papers filed using an overnight delivery service must be addressed:[**]

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* Prior to 6 October 2004, deliver to Crystal Gateway Two, Floor 10, 1225 South Clark Street, Arlington, Virginia.

** Prior to 6 October 2004, use Board of Patent Appeals and Interferences, Crystal Gateway Two, Floor 10, 1225 South Clark Street, Arlington, Virginia.

Board of Patent Appeals and Interferences
Madison Building East, 9th Floor
600 Dulany Street
Alexandria, Virginia 22314

Properly addressed papers filed are deemed filed on the date they are delivered to the overnight delivery service.

¶ 4.4 Telephone calls

Telephone calls to the Board regarding a contested case must be placed to 571-272-9797.[*] A telephone call requesting a conference call must be directed to Trial Section support staff.

¶ 4.5 Facsimile

The facsimile number for contested cases is 571-273-0042.[**] Do not send papers exceeding five (5) pages in length without prior permission from Trial Section support staff.

¶ 5 Copies of authority cited

If a party files a paper citing an authority that is not reported in (1) United States Reports or West Publishing Company's Supreme Court Reporter, (2) the second or third series of West's Federal Reports, or (3) the first or second series of the Bureau of National Affairs' United States Patents Quarterly, then the party must file and serve a copy of the authority.

¶ 6 Modification of the Standing Order

An administrative patent judge may modify the terms of this Order.

¶ 7 Paper format

¶ 7.1 Footnotes

The use of footnotes is discouraged. Footnotes must be double-spaced.

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* Prior to 6 October 2004, use 703-308-9797.

** Prior to 6 October 2004, use 703-305-0942.

¶ 7.2 Cover sheet for papers other than exhibits

¶ 7.2.1 Caption

The heading shown in Part G of the Declaration shall be used in all papers other than exhibits. Form 1 in the Appendix of Forms shows a standard caption for an interference.

¶ 7.2.2 Style

The style of each paper must appear on a single line and must not use the words "et al". Styles for papers other than motions, oppositions, and replies should be simple and descriptive.

¶ 7.2.3 Color of cover sheet

The first page of all papers filed in an contested case must be **pink** similar to the pink first page of the Declaration.

¶ 7.3 Combined oppositions and replies not to be filed

An opposition shall respond to only a single motion and a reply shall respond to only a single opposition.

¶ 7.4 Copy for the administrative patent judge

A party must file (1) an original and (2) a copy of each paper filed. The copy shall be marked at the top:

APJ COPY

¶ 8 Papers in electronic form

¶ 8.1 Only a copy of a paper may be filed in electronic form

Parties may file a copy of a paper in electronic form. (A facsimile is not a paper in electronic form.) The required number of paper copies must also be filed with the Board and served on all opponents.

¶ 8.2 Format

The Board can accept electronic copies in the following PC-compatible media:

A compact disc,

3¼ inch diskette,

A 100 MB Zip® disk, or

A 2 GB Jaz® disk.

The electronic copy must be capable of:

(a) Operating on a computer running WINDOWS XP.

(b) Displaying on a monitor set to display at 256 colors on an 800 x 600 pixel screen setting.

(c) Opening and being word searched in ADOBE ACROBAT READER, WORDPERFECT 9, or MICROSOFT WORD 2000. Parties use other formats at their own risk.

The file name of each electronic document must concisely identify the content of the document (e.g., Jones PM1.wpd, Smith Opp1.doc; Ex1038.pdf). If a hearing is requested, four copies of the electronic media should be filed with the Board and one copy served on each opponent.

¶ 9 Service

¶ 9.1 Alternatives to EXPRESS MAIL®

Any other mode of service that accomplishes a same-day or overnight delivery of the paper (e.g., by hand, facsimile, or a commercial overnight delivery service) may be substituted for EXPRESS MAIL® service.

¶ 9.2 Papers served but not filed

The following papers must be served on an opponent, but should not be filed with the Board at the time of service:

(a) An objection to the admissibility of evidence.

(b) A notice requesting cross-examination.

(c) Automatic discovery pursuant to Bd. R. 150(b)(1).

Such papers may be filed later as an exhibit if a dispute arises with respect to the paper served.

¶ 9.3 Transmittal sheets

Do not file a transmittal sheet listing papers being filed except an exhibit list may be filed when more than one exhibit is being filed.

¶ 10 Lead and backup counsel

The notice identifying counsel under Bd. R. 108(b) must identify both a lead counsel and a backup lead counsel, and must provide for each the contact information specified in Bd. R. 108(b)(1)-(b)(5).

If lead counsel or backup counsel are not counsel of record (37 CFR § 1.34(b)) in the involved application or patent, then a power of attorney must be filed with the Board for entry in the involved patent or application file within the **fourteen (14) day** period of Bd. R. 108(b).

¶ 11 Request for file copies

A party seeking copies of an involved or benefit file mentioned in the Declaration must, within **fourteen (14) days** of the date of the Declaration, file with the Board (not another part of the Office) a separate paper styled [Name of party] REQUEST FOR FILE COPIES to which is attached a completed FILE COPY REQUEST. See Form **4** in the Appendix of Forms.

¶ 12 Later presented or contested claims

If a party moves to involve a new (or uninvolved) claim in the contested case, the movant must comply with the requirements of Bd. R. 110(a) and (b) for the new claim.

¶ 13 Motions

¶ 13.1 Numbering motions

Each motion of each party must be numbered consecutively, starting with one, regardless of the type of motion.

¶ 13.2 Page limits in motions

A motion is limited to twenty-five (25) pages, not including a table of contents, a table of authorities, and the certificate of service.

¶ 13.3 Format

Each motion shall set out in the following order:

(a) The precise relief requested.

(b) The evidence (i.e., a list in numerical order of all exhibits) the movant cites in support of the motion with a brief description of the exhibit (e.g., "Exhibit 1038, Second Declaration of Jones").

(c) A statement of facts in separately numbered paragraphs sufficient to establish entitlement to the requested relief, with citations to the evidence.

(d) An argument setting out the reasons why relief should be granted.

¶ 13.4 Statement of material facts

Facts should be set out as short, numbered declaratory sentences that are capable of being admitted or denied.

Citation to the evidence must be specific, e.g., (1) by column and line of a patent, (2) page, column and paragraph of a journal article and (3) page and line of a cross-examination deposition transcript.

¶ 13.5 Claim chart alternative

As an alternative to a claim chart, a party may reproduce the complete claim in the appendix. Following each limitation in the claim, and within braces { }, insert in bold a specific citation to the information to be compared to the limitation (such as where a prior art reference describes the limitation). Braces { } must be used instead of brackets [ ] because brackets are used to indicate amended portions of claims in reissue applications.

¶ 14 Oppositions and replies

¶ 14.1 Numbering oppositions and replies

Each opposition and reply must use the number of the motion to which it corresponds.

¶ 14.2 Page limits in oppositions and replies

An opposition is limited to twenty-five (25) pages, and a reply is limited to ten (10) pages, not including a table of contents, a table of authorities, and any certificate of service.

¶ 14.3 Opposition format

Each opposition shall set out in the following order:

(a) The evidence (i.e., a list in numerical order of all exhibits by number) the opponent cites in support of the opposition.

(b) For each material fact alleged in the motion, a concise statement admitting, denying, or stating that the opponent is unable to admit or deny the fact.

(c) Any additional material fact upon which the opposition relies, with a citation to the evidence. Any additional material fact must be consecutively numbered beginning with the next number after the last numbered material fact.

(d) An argument stating the reason why relief is opposed shall be made in the following manner:

> On page x, lines y-z of the motion, it is argued (or stated factually) that _. The response is _.

¶ 14.4 Reply format

Each reply shall set out in the following order:

(a) The evidence (i.e., a list in numerical order of all exhibits by number) the movant cites for the first time in support of the reply.

(b) For each material fact alleged in the opposition, a concise statement admitting, denying, or stating that
the movant is unable to admit or deny the fact.

(c) Any additional material fact upon which the movant relies to rebut the opposition, with a citation to the evidence and an explanation as to why each additional material fact was not set out in the motion. Any additional material fact must be consecutively numbered beginning with the next number after the last numbered material fact.

(d) The argument responsive to statements in the opposition shall be made in the following manner:

> On page x, lines y- z of the opposition, it is argued (or stated factually) that _. The response is _.

¶ 15 Miscellaneous motions

¶ 15.1 Mandatory conference call

Before filing a miscellaneous motion, a party must:

(a) confer with all opponents and,

(b) if agreement cannot be reached, arrange a conference call to the Board official administering the contested case.

¶ 15.2 Timeliness

The movant must explain why the motion is timely.

¶ 16 Oral argument

¶ 16.1 Demonstrative exhibits

Four copies (one for the record and one for each judge) of each demonstrative exhibit must be filed or be presented at oral argument. Demonstrative exhibits must be served in advance. Bd. R. 124(d).

Any special equipment needed for oral argument is the responsibility of the party needing the equipment.

¶ 16.2 Transcript of oral argument

When an argument is to be transcribed, the party should notify Trial Section support staff personnel at least one business day prior to oral argument so that arrangements may be made in the hearing room for the reporter.

The court reporter shall use a stenography machine and may also use a tape recording device as a backup. Microphones at individuals' locations are not authorized.

The party requesting transcription must arrange for the transcription and pay the costs. Parties are encouraged to share the costs.

¶ 17 Request for rehearing

¶ 17.1 Form for request

A request for rehearing of decision must set out in the following order:

(a) The evidence (i.e., a list in numerical order of all exhibits by number) that the party believes was overlooked or misapprehended.

(b) The argument responsive to the decision shall be made with particularity in the following manner:

> On page _, lines _-_, the decision states _. The decision is believed to have overlooked [or misapprehended] _. This point was set forth in _ Motion [or Opposition or Reply] _ at page _, lines _-_.

¶ 17.2 Number of requests

A party may file no more than one request for rehearing per motion decision.

¶ 18 Settlement discussions required

¶ 18.1 Last-named party initiates

The party named last on in the caption set in the declaration is responsible for (1) initiating any settlement discussions, (2) initially drafting any document and (3) initiating any conference call required by this paragraph. The parties may agree to permit another party to undertake the obligations placed upon the last-named party.

¶ 18.2 Initial conference

Within **three (3) months** of the date of the Declaration, the parties must conduct a settlement conference and must initiate a conference call with the Board official assigned to the case. During the call, the parties should be prepared to report:

(a) the outcome of the settlement discussion;

(b) whether the parties are actively engaged in settlement negotiations and, if so, what steps have already been taken toward settlement;

(c) whether any settlement negotiations are directed toward obviating the need for filing motions;

(d) any issues that are not subject to settlement negotiations; and

(e) the status of any settlement negotiations, including how much time might be needed to conclude those negotiations.

¶ 18.3 Subsequent conferences

Unless a different time is set in an order, within **two (2) months** after a panel decision on substantive motions, the parties must conduct another settlement conference and initiate another conference call with the Board on the conference as provided in the preceding paragraph of this order.

¶ 18.4 Filing notice of conferences

Prior to initiating any conference call required by this paragraph, the parties must file (preferably by facsimile) a joint statement indicating that a good faith effort has been made to settle the contested case.

¶ 19 Admissibility of specification

A specification of an involved application or patent is admissible as evidence only to prove what the specification or patent describes. If there is data in the specification upon which a party intends to rely to prove the truth of the data, an affidavit by an individual having first-hand knowledge of how the data was generated (i.e., the individual who performed an experiment reported as an example in the specification) must be filed. This individual may be cross examined.

¶ 20 Form of evidence

¶ 20.1 Papers in a patent or application file

¶ 20.1.1 Reliance on a portion of a file

If a motion relies on any paper in the file of an involved or benefit patent or application (including a specification or drawings), a copy of the entire paper shall be made an exhibit in the contested case. Do not submit an entire application file as a single exhibit.

¶ 20.1.2 No exception for affidavits

An affidavit filed during *ex parte* prosecution of an involved or benefit application or patent is not automatically in evidence. A party seeking to have such an affidavit considered must place the affidavit in evidence. Each opponent will have an opportunity to object to the admissibility of the evidence and may cross examine the affiant. The party submitting the evidence will have an opportunity to supplement the evidence following a timely objection by an opponent. Bd. R. 155(b)(2).

¶ 20.2 Exhibit labels

¶ 20.2.1 Unique and consecutive

Each exhibit from a party must be uniquely and consecutively numbered within the range the Board assigns to the party for the proceeding.

Unless otherwise provided in an order, the party named last in the caption set in the declaration is assigned the range 1001-1999, while the first-named party is assigned 2001-2999.

¶ 20.2.2 Material covered on first page

If an exhibit label covers important material on the first page of an exhibit, a copy of the first page of the exhibit must be reproduced and presented as page 1-a of the exhibit.

¶ 20.3 Filing of exhibits

A set of original exhibits must be filed in a box, an accordion folder, or a comparable folder containing the exhibits in numerical order, separated by a divider that conspicuously identifies each exhibit by number.

If any party requests oral argument, three (3) separate additional sets of exhibits must also be filed; otherwise, one (1) additional set of exhibits must be filed.

¶ 20.4 Exhibit list

A current list shall be served whenever evidence is served.

The exhibit list shall be filed with the exhibits.

¶ 21 Objections

¶ 21.1 Objecting to served evidence

An objection to the admissibility of evidence should not be filed except as part of a motion to exclude.

¶ 21.2 Serving supplemental evidence

Supplemental evidence responding to an objection to the admissibility of evidence should not be filed until it is used as an exhibit.

¶ 21.3 Motion to exclude evidence

(a) A motion to exclude evidence shall:

(1) identify where in the record the objection was originally made,

(2) identify where in the record the evidence to be excluded was relied upon by an opponent, and

(3) address objections to exhibits (in whole or in part) in exhibit numerical order.

(b) When a timely objection has been made (see SO **¶ 21.1**), no conference call is necessary to file a motion to exclude.

¶ 22 Cross examination

¶ 22.1 Time for cross examination

The party relying on an affiant must make the affiant available for cross examination during the time required by this Order. The parties must confer to reach agreement on dates and times for cross examination of witnesses.

¶ 22.1.1 Start date

Unless the parties otherwise agree, cross examination of an affiant may begin no earlier than twenty-one (21) days after service of the affidavit.

¶ 22.1.2 End date

Unless the parties otherwise agree,

(1) Cross examination of affiant relied upon in a motion other than a miscellaneous motion must occur at least ten (10) days before the opposition to the motion is due.

(2) Cross examination of an affiant relied upon in an opposition to a motion other than a miscellaneous motion shall take place at least ten (10) days before a reply is due.

¶ 22.2 Notice

A notice requesting cross examination shall be served (but need not be filed).

¶ 22.3 Proponent responsible.

The party relying on an affiant is responsible for securing the services of a court reporter and providing a copy of any transcript to every opponent.

¶ 22.4 Order of cross examination

While a party requesting cross examination may choose the order of the witnesses, Bd. R. 157(c)(2), order must be reasonable.

¶ 22.5 Filing transcript

An uncertified copy of each deposition transcript must be filed as an exhibit. A certified transcript of testimony need not be filed unless required by the Board.

¶ 22.6 Cross examination guidelines

The cross examination guidelines appended to this Order apply to all cross examination in this contested case.

¶ 22.7 Observations on cross examinations

Cross examination may occur after a party has filed its last substantive paper on an issue (e.g., after the reply) and result in testimony that should be called to the Board's attention but does not merit a motion to exclude. The Board may authorize the filing of observations to identify such testimony and responses to observations.

An observation must be a concise statement of the relevance of precisely identified testimony to a precisely identified argument or portion of an exhibit (including another part of the same testimony). Any response should be equally concise. An

observation (or response) is not an opportunity to raise new issues, to re-argue issues, or to pursue objections. Each observation should be in the following form:

> In exhibit _, on page _, lines_, the witness testified _. This testimony is relevant to the _ on page _ of _. The testimony is relevant because _.

The entire observation should not exceed one short paragraph.

¶ 23 Expert testimony on patent law

Affidavits of patent law experts on issues of law generally will not be admitted in evidence.

¶ 24 Explaining tests and data

Any explanation should take place through affidavit testimony of a witness, preferably accompanied by citation to relevant pages of standard texts (which should be filed as exhibits).

¶ 25 Adding an application or patent

A suggestion to add an application or patent to an interference must be in the form of a miscellaneous motion. Bd. R. 121(a)(3). The motion must:

(a) identify the application or patent to be added;

(b) certify that a complete copy of the file wrapper for the application or patent has been served on all opponents;

(c) indicate which claims of the patent or application should be designated as corresponding to the count; and

(d) explain whether there are alternative remedies; if so, why alternative remedies are not adequate; and what attempts, if any, have been made to have the examiner recommend declaration of another interference involving the application or patent sought to be added to the interference.

¶ 26 Motions list

All substantive and anticipated responsive motions must be listed on the motions list. No other substantive motions may be filed without prior Board authorization obtained during a conference call.

¶ 27 Notice under 35 U.S.C. 135(c)

Notice is hereby given of the requirement of 35 U.S.C. 135(c) for filing in the Office a copy of any agreement "in connection with or in contemplation of the termination of the interference."

¶ 28 Specific substantive motions

¶ 28.1 Obviousness

When obviousness (35 U.S.C. 103) is the basis for a motion for judgment, if a reference does not teach or suggest a limitation, that fact must be explicitly identified as a difference in the statement of material facts. The argument portion of the motion must account for the difference.

An explanation must be made in the body of the motion (not an appendix) why the subject matter of the claim, as a whole, would have been obvious to a person having ordinary skill in the art notwithstanding any difference.

¶ 28.2 Inequitable conduct

A motion alleging inequitable conduct must make out a *prima facie* case of inequitable conduct or fraud. Additional discovery (Bd. R. 150(c)) or a request to take testimony (Bd. R. 156), asserted to be necessary to make out a *prima facie* case, will rarely be authorized. An allegation of inequitable conduct or fraud that fails to make out a *prima facie* case may result in sanctions or a referral to the Office of Enrollment and Discipline.

¶ 28.3 Adding a reissue application

A movant seeking to add its own reissue application must stipulate that every added or amended claim (compared to the original patent) corresponds to a count in the interference. If the reissue application has not been filed in the Office, it must be filed directly with the Board.

Entered on 13 September 2004

GARY V. HARKCOM,
Acting Chief Administrative Patent Judge

FRED E. M^{c}KELVEY
Senior Administrative Patent Judge

RICHARD E. SCHAFER
Administrative Patent Judge

JAMESON LEE
Administrative Patent Judge

RICHARD TORCZON
Administrative Patent Judge

CAROL A. SPIEGEL
Administrative Patent Judge

SALLY GARDNER LANE
Administrative Patent Judge

SALLY C. MEDLEY
Administrative Patent Judge

MICHAEL P. TIERNEY
Administrative Patent Judge

JAMES T. MOORE
Administrative Patent Judge

LINDA R. POTEATE
Administrative Patent Judge

MARK NAGUMO
Administrative Patent Judge

BOARD OF
PATENT
APPEALS AND
INTERFERENCES

APPENDIX OF FORMS

Form 1. Standard caption for an interference

Filed on behalf of:
[Name of filing party]
By: [Name of lead counsel]
[Name of backup counsel]
[Street address]
[City, State, and ZIP Code]
[Telephone number]
[Facsimile number]

Paper No. [leave blank]

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES
(Administrative Patent Judge [Surname of administrative patent judge])

[Name of junior party]
([Involved application or patent number])
Junior Party,

v.

[Name of Senior party]
([Involved application or patent number])
Senior Party.

Patent Interference No. [interference number]

[TITLE OF PAPER]

Form 2. Typical schedule for motions

These times typically can be changed by stipulation

TIME PERIOD 1 ..... 6 weeks
File substantive motions
File (but serve one week later) priority statements

TIME PERIOD 2 ..... 3 weeks
File responsive motions to motions
filed in TIME PERIOD 1

TIME PERIOD 3 ..... 6 weeks
File oppositions to all motions

TIME PERIOD 4 ..... 6 weeks
File replies

TIME PERIOD 5 ..... 6 weeks
File request for oral argument
File motions to exclude
File observations

TIME PERIOD 6 ..... 3 weeks
File oppositions to motions to exclude
File response to observations

These times cannot be changed by stipulation

TIME PERIOD 7 ..... 2 weeks
File replies to oppositions to motions to exclude

TIME PERIOD 8 ..... 1 week
File exhibits
File sets of motions

Form 3. Typical schedule for priority motions in an interference

These times typically can be changed by stipulation

TIME PERIOD 9 ..... 6 weeks
Junior party only file priority brief and serve
(but do not file) priority evidence

TIME PERIOD 10 ..... 6 weeks
Senior party only file priority brief and serve
(but do not file) priority evidence

TIME PERIOD 11 ..... 6 weeks
File opposition to priority briefs
Serve (but do not file) opposition evidence

TIME PERIOD 12 ..... 6 weeks
File reply
Serve (but do not file) reply evidence

TIME PERIOD 13 ..... 6 weeks
Request hearing
File list of issues to be considered
File observations
File motion to exclude

TIME PERIOD 14 ..... 3 weeks
File response to observations
File opposition to motion to exclude

The last time cannot be changed by stipulation

TIME PERIOD 15 ..... 2 weeks
File reply to opposition to motion to exclude

TIME PERIOD 16 (Last Time) ..... 1 week
File and serve the exhibits
File sets of priority motions

Form 4. File copy request

FILE COPY REQUEST
Contested Case No. [Contested Case number]

Attach a copy of section E of the DECLARATION to this REQUEST. On the copy, circle each patent and application that you are requesting.

Include the following information to facilitate processing of this REQUEST:

1. Charge fees to USPTO Deposit Account No. _____

2. Complete address, including street, city, state, zip code and telephone number (do not list a Post Office box because file copies are sent by commercial overnight courier).

_____

_____

_____

_____

3. Telephone, including area code: _____

APPENDIX: CROSS EXAMINATION GUIDELINES

Introduction

Cross examination can be a useful tool for determining the facts in a case. In contested cases, direct testimony is usually presented by affidavit, Bd. R. 157(a), while cross examination occurs by oral deposition. Bd. R. 157(b).

Cross examination should be a question-and-answer conversation between the examining lawyer and the witness. The defending lawyer must not act as an intermediary, interpreting questions, deciding which questions the witness should answer and helping the witness formulate answers. The witness comes to the cross examination to be questioned. It is the witness, and not the lawyer, who is testifying.

The cross-examination guidelines below are essentially the deposition guidelines set out in *Hall v. Clifton Precision*, 150 F.R.D. 525 (E.D. Pa. 1993) (Gawthrop, J.) The only significant difference, which results from Bd. R. 157(e)(4), is that certain objections must be noted on the record.

Failure to adhere strictly to these guidelines may be a basis for a sanction under Bd. R. 128, which could include a requirement that the witness, on very short notice may be directed to appear before the Board or elsewhere, as may be appropriate, coupled with any appropriate award of compensatory damages under Bd. R. 128(b)(6). In addition, cross examination undertaken contrary to these guidelines may result in exclusion of an affidavit from evidence or in the assignment of little, if any weight, to the direct testimony of a witness who was cross examined.

Guideline [1]

At the beginning of a cross examination, the party conducting the cross examination must instruct the witness on the record to ask deposing counsel, rather than the witness's own counsel, for clarifications, definitions or explanations of any words,

questions or documents presented during the cross examination. The witness must follow these instructions.

Guideline [2]

A party may not direct or request that a witness not answer a question unless:

(a) a party has objected to the question on the ground that the answer would:

(1) reveal privileged material or

(2) violate a limitation the Board has imposed and

(b) counsel immediately places a conference call to the Board official assigned to the contested case asking for a ruling on the objection.

Under these circumstances, (i) the cross examination shall be suspended, (ii) the conference call immediately shall be placed to the Board official assigned to the contested case, and (iii) all counsel must be prepared to explain their respective positions during the call. The court reporter for the cross examination shall be available to record the conference call and to read back questions to which an objection has been made.

If the Board cannot be reached, then the party directing a witness not to answer shall, within **two (2) business days**, deliver by hand (SO ¶ **4.2**), overnight service (SO ¶ **4.3**), or facsimile (SO ¶ **4.5**) directly to the Board, and not to the Office Mail Room or any other part of the Office, a miscellaneous motion seeking relief. Bd. R. 121(a)(3). Any opposition must be hand delivered to the Board within **two (2) business days** of service of the motion. While a reply can be filed, the motion is likely to be decided before it is filed.

Guideline [3]

Counsel must not make objections or statements that even remotely suggest an answer to a witness. Any objection to evidence during cross examination must be stated concisely and in a non-argumentative and non-suggestive manner and must include the legal basis for the objection. Examining counsel must not address the correctness of an objection, but may instead continue with questions to the witness, the objection having been noted on the record as required under Bd. R. 157(e)(4).*

Guideline [4]

Counsel and their witness-clients shall not engage in private, off-the-record conferences during cross examinations or during breaks or recesses, except for the purpose of deciding whether to assert a privilege.**

---

* With respect to this guideline, the following observation by Judge Gawthrop, 150 F.R.D. at 530 n.10, is highly relevant:

> I also note that a favorite objection or interjection of lawyers is, "I don't understand the question; therefore the witness doesn't understand the question." This is not a proper objection. If the witness needs clarification, the witness may ask the deposing lawyer for clarification. A lawyer's purported lack of understanding is not a proper reason to interrupt a deposition. In addition, counsel are not permitted to state on the record their interpretations of questions, since those interpretations are irrelevant and often suggestive of a particularly desired answer.

By way of example, the following comments by defending counsel generally are viewed as suggesting an answer to a witness:

(a) Objection, vague.
(b) Objection to the form of the question.
(c) Take your time in answering the question.
(d) Look at the document before you answer.
(e) Counsel, do you want to show the witness the document?

** The term "witness-clients" in the context of this guideline includes all witnesses who are employed by, or otherwise under the control of, the real party-in-interest, including retained expert witnesses, as well as the individual or individuals named in the caption of the contested case. With respect to this guideline, the following observation by Judge Gawthrop, 150 F.R.D. at 528, is highly relevant:

> The fact that there is no judge in the room to prevent private conferences does not mean that such conferences should or may occur. The underlying reason for preventing private conferences is still present: they tend, at the very least, to give the appearance of obstructing the truth.

Guideline [5]

Any conferences that occur pursuant to, or in violation of, guideline [4] are a proper subject for inquiry by deposing counsel to ascertain whether there has been any witness-coaching and, if so, the nature of that coaching.

Guideline [6]

Any conferences that occur pursuant to, or in violation of, guideline [4] shall be noted on the record by the counsel who participated in the conference. The purpose and outcome of the conference shall also be noted on the record.

Guideline [7]

Counsel taking cross-examination shall provide to defending counsel a copy of all documents shown to the witness during the cross examination. The copies shall be provided either before the cross examination begins or contemporaneously with the showing of each document to the witness. The witness and defending counsel do not have a right to discuss documents privately before the witness answers questions about the documents.

APPENDIX: INDEX OF TIMES

Times running from initiation/declaration

Notice of lead and backup counsel (Bd. R. 108(b)) ..... 14 days

Clean copy of claims (Bd. R. 110(a)) ..... 14 days

Notice of real party-in-interest (SO ¶ **3.1**) ..... 14 days

Notice of related proceedings (SO ¶ **3.2**) ..... 14 days

Request for file copies (SO ¶ **11**) ..... 14 days

Annotated copy of claims (Bd. R. 110(b)) ..... 28 days

Notice of confidential information (SO ¶ **1**) ..... 2 months

Initial settlement conference (SO ¶ **18.2**) ..... 3 months

Default times before a triggering event

Service of demonstrative exhibit for oral argument (Bd. R. 124(d)) ... 5 business days

Notice of transcription of oral argument (SO ¶ **16.2**) ..... 1 business day

End of cross examination before opposition or reply (SO ¶ **22.1.2**) ..... 10 days

List of documents and things for cross examination before conference call (Bd. R. 157(c)(3)) ..... 3 business days

Notice of deposition (Bd. R. 157(c)(4)) ..... 2 business days

Conference call regarding interpreter for deposition (Bd. R. 157(d)) .. 5 business days